REMARKS

The above amendments to the above-captioned application along with the following remarks are being submitted as a full and complete response to the Official Action dated April 8, 2003, and the phone interview with Examiner on June 12, 2003.

Claims 2 and 4 are under consideration in this application. Claims 1 and 3 are being cancelled without prejudice or disclaimer. Claims 2 and 4 are being amended, as set forth above and in the attached marked-up presentation of the claim amendments, in order to more particularly define and distinctly claim applicants' invention. Applicants hereby submit that no new matter is being introduced into the application through the submission of this response.

In view of the above amendments and the following remarks, the Examiner is respectfully requested to give due reconsideration to this application, to indicate the allowability of the claims, and to pass this case to issue.

Formality Rejection

The recitation of "said primers" in the claims 1-4 was rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. As indicated, the recitation has been amended as required by the Examiner. Accordingly, the withdrawal of the outstanding informality rejection is in order, and is therefore respectfully solicited.

Prior Art Rejections

Claims 1-4 were rejected under 35 U.S.C. § 102(b) as being anticipated by an article written by Schollien et al. (Clinical Chemistry, Vol. 43, No. 1, pp.18-23, 1997, herein after "Schollien"), and further rejection under 35 U.S.C. § 103(a) as being unpatentable over Schollien in view of U.S. Pat. No. 5,232,829 to Longiaru et al. (hereinafter "Longiaru"). These rejections have been carefully considered, but are most respectfully traversed.

The method of detecting PCR-amplified base sequences 42 of the invention, as now recited in claim 2, comprises: conducting PCR amplification by mixing a plurality of primer pairs with a sample, said primer pairs being suitable for amplifying different base sequences, such as

DNA (1), DNA(2), of a same length or different lengths by PCR; conducting a hybridization reaction by using a substrate 30 on which one primer of each of said primer pairs used for the PCR (e.g., primers 31, 32, 33 which are three types of forward primers of the same length, page 9, lines 7, 12-26, Fig. 3), are fixedly spotted on spots thereon and a solution containing said base sequences that are PCR-amplified in the preceding step, said hybridization reaction being performed between the primers fixedly spotted on the substrate and said PCR-amplified base sequences; and detecting at least one of the spots on said substrate in which the hybridization reaction occurs. Different types of primers 31, 32, 33 (which may be of the same length) are fixed/implanted on different spots of a glass slide/ substrate 30 (page 9, lines 15-18) to hybridize with different types of DNAs so as to measure the fluorescence emitted from each spot corresponding to one type of PCR-amplified DNAs 42 derived from a respective type of primer (page 10, lines 25-28) and thereby determine the amount of different types of PCR-amplified DNAs . In particular, the spot detecting step involves (1) processing a fluorescent material 46 to enter in said PCR-amplified base sequences 42 which are double-stranded DNAs (page 10, lines 10-28; Fig. 4); and (2) detecting fluorescence generated by exciting said fluorescent material contained in said at least one of the spots on the substrate.

Applicants respectfully contend that neither Schollien nor Longiaru, nor their combination as relied upon by the Examiner, teaches or suggests "entering a fluorescent material 46 in said PCR-amplified double-stranded DNAs 42" thereby corresponding one fluorescent regent 46 with one PCR-amplified double-stranded DNA 42.

In contrast, Schollien requires the use of **biotinylated** primers (page 19, col. 1, line 26) and the detection is conducted with chemiluminescence (Abstract, line 9), i.e., emission of light as a result of a chemical reaction at environmental temperatures[1]. Longiaru also requires the use of **biotin-labeled** DNAs (see SUMMARY OF THE INVENTION in column 3). In other words, both references require the use of biotin-labeled primers or DNAs. Biotin-labeling requires utilizing heat- or light- activation to rapidly and *covalently (chemically)* attach labels to nucleic acids, rather simply *entering* a fluorescent material in a PCR-amplified DNA's *double-stranded* structure as the invention. In addition, the biotin-labeled primers or DNAs are chemically different form the non-biotin-labeled primers or DNAs used according to the invention such that

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[1] *The American Heritage® Dictionary of the English Language, Third Edition* copyright © 1992 by Houghton Mifflin Company.

their interference with PCR or hybridization reactions makes it impossible to conduct accurate measurement of the PCR-amplification products.

Applicants respectfully caution the Examiner that any reliance upon the "common knowledge and common sense" of one skilled in the art for motivation to combine the teachings in Schollien or Longiaru with a teaching of "entering a fluorescent material in a PCR-amplified double-stranded DNA" has to fulfill the agency's obligation to cite references, e.g. explicit *statements in the prior art*, to support its conclusions on the record to allow accountability.

> *To establish a prima facie case of obviousness, the Board must, inter alia, show "some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references." In re Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988). "The motivation, suggestion or teaching may come explicitly from statements in the prior art, the knowledge of one of ordinary skill in the art, or, in some cases the nature of the problem to be solved." Kotzab, 217 F.3d at 1370, 55 USPQ2d at 1317. .... Recently, in In re Lee, 277 F.3d 1338, 61 USPQ2d 1430 (Fed. Cir. 2002), we held that the Board's reliance on "common knowledge and common sense" did not fulfill the agency's obligation to cite references to support its conclusions. Id. at 1344, 61 USPQ2d at 1434. Instead, the Board must document its reasoning on the record to allow accountability. Id. at 1345, 61 USPQ2d at 1435.*
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> See In re Thrift, 298 F.3d 1357.

Applicants will contend that neither Schollien, Longiaru, nor their combination teaches or discloses each and every feature of the present invention as disclosed in at least independent claim 1. As such, the present invention as now claimed is distinguishable and thereby allowable over the rejections raised in the Office Action. The withdrawal of the outstanding prior art rejections is in order, and is respectfully solicited.

In view of all the above, clear and distinct differences as discussed exist between the present invention as now claimed and the prior art reference upon which the rejections in the Office Action rely, Applicants respectfully contend that the prior art references cannot anticipate the present invention or render the present invention obvious. Rather, the present invention as a whole is distinguishable, and thereby allowable over the prior art.

Favorable reconsideration of this application is respectfully solicited. Should there be any outstanding issues requiring discussion that would further the prosecution and allowance of the above-captioned application, the Examiner is invited to contact the Applicants' undersigned representative at the address and phone number indicated below.

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Marked-up Version of Amended Claims

2. [The] A method of detecting PCR-amplified base sequences [according to claim 1], comprising the steps of:

conducting PCR amplification by mixing a plurality of primer pairs with a sample, said primer pairs being suitable for amplifying different base sequences of a same length or different lengths by PCR;

conducting a hybridization reaction by using a substrate on which one primer of each of said primer pairs used for the PCR are fixedly spotted on spots thereon and a solution containing said base sequences that are PCR-amplified in the preceding step, said hybridization reaction being performed between the primers fixedly spotted on the substrate and said PCR-amplified base sequences; and

detecting at least one of the spots on said substrate in which the hybridization reaction occurs,

wherein said step of detecting the spots on said substrate in which the hybridization reaction occurs includes the steps of:

processing a fluorescent material to enter in said PCR-amplified base sequences which are double-stranded DNAs; and

detecting fluorescence generated by exciting said fluorescent material contained in said at least one of the spots on the substrate.